

SEQUENCE LISTING

<110> Merck & Co., Inc.
Steinkuhler, Christian
Lahm, Armin
Pallaoro, Michele
Nardella, Caterina

<120> SYNTHETIC HEPARANASE MOLECULES AND USES
THEREOF

<130> ITR0060Y-PCT

<150> 60/537,729

<151> 2004-01-20

<150> 60/506,479

<151> 2003-09-26

<160> 44

<170> FastSEQ for Windows Version 4.0

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 caggagcaat tg 72
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 <212> DNA
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 <223> PCR Primer
 <400> 9
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 gagcaattg 69

<210> 10
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Peptide

<400> 10
 Glu Gly Ser Gly Ser Glu Asn Leu Tyr Phe Gln Gly Ser Gly Gly
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<210> 11
 <211> 63
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 11
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 tac 63

<210> 12
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Peptide

<400> 12
 Gln Gly Ser Gly Ser Glu Asn Leu Tyr Phe Gln Gly Ser Gly Ser Lys
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<210> 13
 <211> 66
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR Primer

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<210> 14
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Peptide

<400> 14
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 Gln

<210> 15
 <211> 74
 <212> PRT
 <213> Human

<400> 15
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 Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn Leu Ala Thr
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 35 40 45
 Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr
 50 55 60
 Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu
 65 70

<210> 16
 <211> 386
 <212> PRT
 <213> Human

<400> 16
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 35 40 45
 Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu
 50 55 60
 Leu Gly Asn Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile
 65 70 75 80
 Asn Gly Ser Gln Leu Gly Glu Asp Phe Ile Gln Leu His Lys Leu Leu
 85 90 95
 Arg Lys Ser Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly
 100 105 110
 Gln Pro Arg Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala
 115 120 125
 Gly Gly Glu Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn
 130 135 140
 Gly Arg Thr Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp
 145 150 155 160
 Ile Phe Ile Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr
 165 170 175
 Arg Pro Gly Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly
 180 185 190
 Gly Gly Ala Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp
 195 200 205
 Leu Asp Lys Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met
 210 215 220
 Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn
 225 230 235 240
 Phe Asp Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu
 245 250 255
 Val Gly Thr Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg
 260 265 270
 Lys Leu Arg Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr
 275 280 285
 Lys Glu Gly Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr
 290 295 300
 Lys Tyr Leu Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys

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305          310          315          320
Tyr Leu Leu Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val
          325          330          335
Gln Leu Asn Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro
          340          345          350
Pro Leu Met Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro
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Cys Ile
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<210> 17
<211> 492
<212> PRT
<213> Artificial Sequence

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<220>
<223> hep 106

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Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro
          35          40          45
Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn
          50          55          60
Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu
65          70          75          80
Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly
          85          90          95
Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Phe Lys Asn Ser
          100          105          110
Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe Ala Asn Cys
          115          120          125
Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Ala
          130          135          140
Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys
145          150          155          160
Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn
          165          170          175
Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser Gln Leu Gly
          180          185          190
Glu Asp Phe Ile Gln Leu His Lys Leu Leu Arg Lys Ser Thr Phe Lys
          195          200          205
Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg Arg Lys Thr
          210          215          220
Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp
225          230          235          240
Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr Ala Thr Arg
          245          250          255
Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe Ile Ser Ser Val
          260          265          270
Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro Gly Lys Lys Val
          275          280          285
Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu
          290          295          300
Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu
305          310          315          320
Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln Val Phe Phe Gly
          325          330          335

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Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp Pro Leu Pro Asp
 Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly Thr Lys Val Leu
 Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu Arg Val Tyr Leu
 His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly Asp Leu Thr
 Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr Leu Arg Leu Pro
 Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu Leu Arg Pro Leu
 Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu Asn Gly Leu Thr
 Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu Met Glu Lys Pro
 Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe Ser Tyr Ser Phe
 Phe Val Ile Arg Asn Ala Lys Val Ala Ala Cys Ile

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 370 375 380
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 405 410 415
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 485 490

<210> 18
 <211> 1479
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> hep 106

<400> 18
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 ctggacttct tcacccagga gccgctgcac ctggtagagc cctcgttcct gtccgtcacc 180
 attgacgcca acctggccac ggacccgcgg ttccctcatcc tcctgggttc tccaaagctt 240
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 gtgctataca cttttgcaaa ctgctcagga ctggacttga tctttggcct aaatgcgtta 420
 ttaagaacag cagatttgca gtggaacagt tctaattgctc agttgctcct ggactactgc 480
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<210> 19
 <211> 1488
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> hep 109

<400> 19

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<210> 20

<211> 495

<212> PRT

<213> Artificial Sequence

<220>

<223> hep 109

<400> 20

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Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro
35      40      45
Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn
50      55      60
Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu
65      70      75      80
Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly
85      90      95
Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Lys Lys Phe
100     105     110
Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe
115     120     125
Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu
130     135     140
Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu
145     150     155     160
Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn
165     170     175
Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser
180     185     190
Gln Leu Gly Glu Asp Phe Ile Gln Leu His Lys Leu Leu Arg Lys Ser
195     200     205
Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg

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210	Arg	Lys	Thr	Ala	Lys	Met	Leu	Lys	Ser	Phe	Leu	Lys	Ala	Gly	Gly	Glu
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	Ser	Ser	Val	Gln	Lys	Val	Phe	Gln	Val	Val	Glu	Ser	Thr	Arg	Pro	Gly
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	Lys	Lys	Val	Trp	Leu	Gly	Glu	Thr	Ser	Ser	Ala	Tyr	Gly	Gly	Gly	Ala
				290					295							
	Pro	Leu	Leu	Ser	Asp	Thr	Phe	Ala	Ala	Gly	Phe	Met	Trp	Leu	Asp	Lys
									310							
	Leu	Gly	Leu	Ser	Ala	Arg	Met	Gly	Ile	Glu	Val	Val	Met	Arg	Gln	Val
					325					330						
	Phe	Phe	Gly	Ala	Gly	Asn	Tyr	His	Leu	Val	Asp	Glu	Asn	Phe	Asp	Pro
				340					345							
	Leu	Pro	Asp	Tyr	Trp	Leu	Ser	Leu	Leu	Phe	Lys	Lys	Leu	Val	Gly	Thr
				355					360							
	Lys	Val	Leu	Met	Ala	Ser	Val	Gln	Gly	Ser	Lys	Arg	Arg	Lys	Leu	Arg
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	Val	Tyr	Leu	His	Cys	Thr	Asn	Thr	Asp	Asn	Pro	Arg	Tyr	Lys	Glu	Gly
	Asp	Leu	Thr	Leu	Tyr	Ala	Ile	Asn	Leu	His	Asn	Val	Thr	Lys	Tyr	Leu
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	Arg	Leu	Pro	Tyr	Pro	Phe	Ser	Asn	Lys	Gln	Val	Asp	Lys	Tyr	Leu	Leu
				420					425							
	Arg	Pro	Leu	Gly	Pro	His	Gly	Leu	Leu	Ser	Lys	Ser	Val	Gln	Leu	Asn
				435					440							
	Gly	Leu	Thr	Leu	Lys	Met	Val	Asp	Asp	Gln	Thr	Leu	Pro	Pro	Leu	Met
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	Glu	Lys	Pro	Leu	Arg	Pro	Gly	Ser	Ser	Leu	Gly	Leu	Pro	Ala	Phe	Ser
	Tyr	Ser	Phe	Phe	Val	Ile	Arg	Asn	Ala	Lys	Val	Ala	Ala	Cys	Ile	
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<210> 21
 <211> 501
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> hep GS3

<400> 21
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 35 40 45
 Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn
 50 55 60
 Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu
 65 70 75 80
 Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly
 85 90 95
 Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Gly Ser Gly
 100 105 110
 Ser Gly Ser Lys Lys Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val
 115 120 125
 Asp Val Leu Tyr Thr Phe Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe
 130 135 140

Gly Leu Asn Ala Leu Leu Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser
 145 150 155 160
 Asn Ala Gln Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile
 165 170 175
 Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp
 180 185 190
 Ile Phe Ile Asn Gly Ser Gln Leu Gly Glu Asp Phe Ile Gln Leu His
 195 200 205
 Lys Leu Leu Arg Lys Ser Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro
 210 215 220
 Asp Val Gly Gln Pro Arg Arg Lys Thr Ala Lys Met Leu Lys Ser Phe
 225 230 235 240
 Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Val Thr Trp His His Tyr
 245 250 255
 Tyr Leu Asn Gly Arg Thr Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp
 260 265 270
 Val Leu Asp Ile Phe Ile Ser Ser Val Gln Lys Val Phe Gln Val Val
 275 280 285
 Glu Ser Thr Arg Pro Gly Lys Lys Val Trp Leu Gly Glu Thr Ser Ser
 290 295 300
 Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly
 305 310 315 320
 Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Arg Met Gly Ile Glu
 325 330 335
 Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His Leu Val
 340 345 350
 Asp Glu Asn Phe Asp Pro Leu Pro Asp Tyr Trp Leu Ser Leu Phe
 355 360 365
 Lys Lys Leu Val Gly Thr Lys Val Leu Met Ala Ser Val Gln Gly Ser
 370 375 380
 Lys Arg Arg Lys Leu Arg Val Tyr Leu His Cys Thr Asn Thr Asp Asn
 385 390 395 400
 Pro Arg Tyr Lys Glu Gly Asp Leu Thr Leu Tyr Ala Ile Asn Leu His
 405 410 415
 Asn Val Thr Lys Tyr Leu Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln
 420 425 430
 Val Asp Lys Tyr Leu Leu Arg Pro Leu Gly Pro His Gly Leu Leu Ser
 435 440 445
 Lys Ser Val Gln Leu Asn Gly Leu Thr Leu Lys Met Val Asp Asp Gln
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 Thr Leu Pro Pro Leu Met Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu
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<210> 22

<211> 1506

<212> DNA

<213> Artificial Sequence

<220>

<223> hep GS3

<400> 22

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gtggatgac aaaccttgcc acctttaatg gaaaaacctc tccggccagg aagttcactg 1440
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<210> 23

<211> 1584

<212> DNA

<213> Artificial Sequence

<220>

<223> hep GS4

<400> 23

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ctggacttct tcacccagga gccgctgcac ctggtgagcc cctcgttcct gtccgtcacc 180
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cagaaaaagt tcaagaacag cacctactca agaagctctg tagatgtgct atacactttt 480
gcaaaactgc caggactgga cttgatcttt ggcctaaatg cgttattaag aacagcagat 540
ttgcagtggg acagttctaa tgctcagttg ctctcggact actgctcttc caaggggtat 600
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atcaatgggt cgcagttagg agaagatttt attcaattgc ataaacttct aagaaagtcc 720
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<210> 24

<211> 1524

<212> DNA

<213> Artificial Sequence

<220>

<223> hep GS6

<400> 24

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aagatgctga agagcttcct gaaggctggt ggagaagtga ttgattcagt tacatggcat 780
cactactatt tgaatggacg gactgctacc agggaagatt ttctaaacct tgatgtattg 840
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aagaaggtct ggttaggaga aacaagctct gcatatggag gcggagcgcc cttgctatcc 960
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<210> 25

<211> 527

<212> PRT

<213> Artificial Sequence

<220>

<223> hep GS-A4

<400> 25

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20      25      30
Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro
35      40      45
Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn
50      55      60
Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu
65      70      75      80
Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly
85      90      95
Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr Phe
100      105      110
Glu Glu Arg Ser Tyr Trp Gly Ser Gly Ala Gly Ser Gly Ala Glu Trp
115      120      125
Pro Tyr Gln Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys Phe
130      135      140
Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe
145      150      155      160
Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu
165      170      175
Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu
180      185      190
Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn
195      200      205

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Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser
 210 215 220
 Gln Leu Gly Glu Asp Phe Ile Gln Leu His Lys Leu Leu Arg Lys Ser
 225 230 235 240
 Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg
 245 250 255
 Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu
 260 265 270
 Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr
 275 280 285
 Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe Ile
 290 295 300
 Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro Gly
 305 310 315 320
 Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala
 325 330 335
 Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp Lys
 340 345 350
 Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln Val
 355 360 365
 Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp Pro
 370 375 380
 Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly Thr
 385 390 395 400
 Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu Arg
 405 410 415
 Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly
 420 425 430
 Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr Leu
 435 440 445
 Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu Leu
 450 455 460
 Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu Asn
 465 470 475 480
 Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu Met
 485 490 495
 Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe Ser
 500 505 510
 Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala Cys Ile
 515 520 525

<210> 26

<211> 507

<212> PRT

<213> Artificial Sequence

<220>

<223> hep GS-A6

<400> 26

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 20 25 30
 Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro
 35 40 45
 Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn
 50 55 60
 Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu
 65 70 75 80
 Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly
 85 90 95
 Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Gly Ser Gly

Ser	Gly	Ser	100	Gly	Ser	Gly	Ser	105	Gly	Ser	Lys	Lys	Phe	Lys	110	Asn	Ser	Thr
Tyr	Ser	Arg	115	Ser	Ser	Val	Asp	120	Val	Leu	Tyr	Thr	Phe	125	Ala	Asn	Cys	Ser
Gly	Leu	Asp	130	Leu	Ile	Phe	Gly	135	Leu	Asn	Ala	Leu	Leu	140	Arg	Thr	Ala	Asp
Leu	Gln	Trp	145	Asn	Ser	150	Asn	155	Ala	Gln	Leu	Leu	Leu	160	Asp	Tyr	Cys	Ser
Ser	Lys	Gly	165	Tyr	Asn	170	Ile	175	Ser	Trp	Glu	Leu	Gly	180	Asn	Glu	Pro	Asn
Phe	Leu	Lys	185	Lys	Ala	Asp	Ile	190	Phe	Ile	Asn	Gly	Ser	195	Gln	Leu	Gly	Glu
Asp	Phe	Ile	200	Gln	Leu	His	Lys	205	Leu	Leu	Arg	Lys	Ser	210	Thr	Phe	Lys	Asn
Ala	Lys	Leu	215	Tyr	Gly	Pro	Asp	220	Val	Gly	Gln	Pro	Arg	225	Arg	Lys	Thr	Ala
Lys	Met	Leu	230	Lys	Ser	235	Phe	240	Leu	Lys	Ala	Gly	Gly	245	Glu	Val	Ile	Asp
Val	Thr	Trp	250	His	His	255	Tyr	260	Tyr	Leu	Asn	Gly	Arg	265	Thr	Ala	Thr	Arg
Asp	Phe	Leu	270	Asn	Pro	275	Asp	280	Val	Leu	Asp	Ile	Phe	285	Ile	Ser	Ser	Val
Lys	Val	Phe	290	Gln	Val	295	Val	300	Glu	Ser	Thr	Arg	Pro	305	Gly	Lys	Lys	Val
Leu	Gly	Glu	310	Thr	Ser	315	Ser	320	Ala	Tyr	Gly	Gly	Gly	325	Ala	Pro	Leu	Leu
Asp	Thr	Phe	330	Ala	Ala	335	Gly	340	Phe	Met	Trp	Leu	Asp	345	Lys	Leu	Gly	Leu
Ala	Arg	Met	350	Gly	Ile	355	Glu	360	Val	Val	Met	Arg	Gln	365	Val	Phe	Phe	Gly
Gly	Asn	Tyr	370	His	Leu	375	Val	380	Asp	Glu	Asn	Phe	Asp	385	Pro	Leu	Pro	Asp
Trp	Leu	Ser	390	Leu	Leu	395	Phe	400	Lys	Lys	Leu	Val	Gly	405	Thr	Lys	Val	Leu
Ala	Ser	Val	410	Gln	Gly	415	Ser	420	Arg	Arg	Lys	Leu	Arg	425	Val	Tyr	Leu	His
Cys	Thr	Asn	430	Thr	Asp	435	Asn	440	Pro	Arg	Tyr	Lys	Glu	445	Gly	Asp	Leu	Thr
Tyr	Ala	Ile	450	Asn	Leu	455	His	460	Asn	Val	Thr	Lys	Tyr	465	Leu	Arg	Leu	Pro
Pro	Phe	Ser	470	Asn	Lys	475	Gln	480	Val	Asp	Lys	Tyr	Leu	485	Leu	Arg	Pro	Leu
Pro	His	Gly	490	Leu	Leu	495	Ser	500	Val	Gln	Ser	Val	Gln	505	Leu	Asn	Gly	Leu
Lys	Met	Val	510	Asp	Asp	515	Gln	520	Thr	Leu	Pro	Pro	Leu	525	Met	Glu	Lys	Pro
Arg	Pro	Gly	530	Ser	Ser	535	Leu	540	Gly	Leu	Pro	Ala	Phe	545	Ser	Tyr	Ser	Phe
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<210> 27

<211> 526

<212> PRT

<213> Artificial Sequence

<220>

<223> hep Hyal

<400> 27

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			20					25					30		
Ala	Gln	Ala	Gln	Asp	Val	Val	Asp	Leu	Asp	Phe	Phe	Thr	Gln	Glu	Pro
		35					40					45			
Leu	His	Leu	Val	Ser	Pro	Ser	Phe	Leu	Ser	Val	Thr	Ile	Asp	Ala	Asn
	50					55					60				
Leu	Ala	Thr	Asp	Pro	Arg	Phe	Leu	Ile	Leu	Leu	Gly	Ser	Pro	Lys	Leu
65					70					75				80	
Arg	Thr	Leu	Ala	Arg	Gly	Leu	Ser	Pro	Ala	Tyr	Leu	Arg	Phe	Gly	Gly
			85						90					95	
Thr	Lys	Thr	Asp	Phe	Leu	Ile	Phe	Asp	Pro	Lys	Lys	Glu	Ser	Thr	Phe
			100					105					110		
Glu	Glu	Arg	Ser	Tyr	Trp	Ala	Phe	Lys	Asp	Lys	Thr	Pro	Glu	Trp	Pro
		115					120					125			
Tyr	Gln	Glu	Gln	Leu	Leu	Leu	Arg	Glu	His	Tyr	Gln	Lys	Lys	Phe	Lys
	130					135					140				
Asn	Ser	Thr	Tyr	Ser	Arg	Ser	Ser	Val	Asp	Val	Leu	Tyr	Thr	Phe	Ala
145					150					155					160
Asn	Cys	Ser	Gly	Leu	Asp	Leu	Ile	Phe	Gly	Leu	Asn	Ala	Leu	Leu	Arg
			165						170					175	
Thr	Ala	Asp	Leu	Gln	Trp	Asn	Ser	Ser	Asn	Ala	Gln	Leu	Leu	Leu	Asp
		180						185					190		
Tyr	Cys	Ser	Ser	Lys	Gly	Tyr	Asn	Ile	Ser	Trp	Glu	Leu	Gly	Asn	Glu
		195					200					205			
Pro	Asn	Ser	Phe	Leu	Lys	Lys	Ala	Asp	Ile	Phe	Ile	Asn	Gly	Ser	Gln
	210					215					220				
Leu	Gly	Glu	Asp	Phe	Ile	Gln	Leu	His	Lys	Leu	Leu	Arg	Lys	Ser	Thr
225					230					235					240
Phe	Lys	Asn	Ala	Lys	Leu	Tyr	Gly	Pro	Asp	Val	Gly	Gln	Pro	Arg	Arg
			245						250					255	
Lys	Thr	Ala	Lys	Met	Leu	Lys	Ser	Phe	Leu	Lys	Ala	Gly	Gly	Glu	Val
		260						265					270		
Ile	Asp	Ser	Val	Thr	Trp	His	His	Tyr	Tyr	Leu	Asn	Gly	Arg	Thr	Ala
		275					280					285			
Thr	Arg	Glu	Asp	Phe	Leu	Asn	Pro	Asp	Val	Leu	Asp	Ile	Phe	Ile	Ser
	290					295					300				
Ser	Val	Gln	Lys	Val	Phe	Gln	Val	Val	Glu	Ser	Thr	Arg	Pro	Gly	Lys
					310					315					320
Lys	Val	Trp	Leu	Gly	Glu	Thr	Ser	Ser	Ala	Tyr	Gly	Gly	Gly	Ala	Pro
			325						330					335	
Leu	Leu	Ser	Asp	Thr	Phe	Ala	Ala	Gly	Phe	Met	Trp	Leu	Asp	Lys	Leu
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Gly	Leu	Ser	Ala	Arg	Met	Gly	Ile	Glu	Val	Val	Met	Arg	Gln	Val	Phe
		355				360						365			
Phe	Gly	Ala	Gly	Asn	Tyr	His	Leu	Val	Asp	Glu	Asn	Phe	Asp	Pro	Leu
	370					375					380				
Pro	Asp	Tyr	Trp	Leu	Ser	Leu	Leu	Phe	Lys	Lys	Leu	Val	Gly	Thr	Lys
385					390					395					400
Val	Leu	Met	Ala	Ser	Val	Gln	Gly	Ser	Lys	Arg	Arg	Lys	Leu	Arg	Val
			405						410					415	
Tyr	Leu	His	Cys	Thr	Asn	Thr	Asp	Asn	Pro	Arg	Tyr	Lys	Glu	Gly	Asp
			420					425					430		
Leu	Thr	Leu	Tyr	Ala	Ile	Asn	Leu	His	Asn	Val	Thr	Lys	Tyr	Leu	Arg
		435				440						445			
Leu	Pro	Tyr	Pro	Phe	Ser	Asn	Lys	Gln	Val	Asp	Lys	Tyr	Leu	Leu	Arg
	450					455					460				
Pro	Leu	Gly	Pro	His	Gly	Leu	Leu	Ser	Lys	Ser	Val	Gln	Leu	Asn	Gly
465					470					475					480
Leu	Thr	Leu	Lys	Met	Val	Asp	Asp	Gln	Thr	Leu	Pro	Pro	Leu	Met	Glu
			485						490					495	
Lys	Pro	Leu	Arg	Pro	Gly	Ser	Ser	Leu	Gly	Leu	Pro	Ala	Phe	Ser	Tyr
			500					505					510		
Ser	Phe	Phe	Val	Ile	Arg	Asn	Ala	Lys	Val	Ala	Ala	Cys	Ile		
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<210> 28
 <211> 1581
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> hep Hyal

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 cgtaccttgg ccagaggctt gtctcctgcg tacctgaggt ttgggtggcac caagacagac 300
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 aaggacaaga ccccggaatg gccctaccag gagcaattgc tactccgaga acactaccag 420
 aaaaagtcca agaacagcac ctactcaaga agctctgtag atgtgctata cacttttgca 480
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 aatgggtcgc agttaggaga agattttatt caattgcata aacttctaag aaagtccacc 720
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 gaagtgggtg taggcaagt attctttgga gcaggaaact accatttagt ggatgaaaac 1140
 ttcgatcctt tacctgatta ttggctatct cttctgttca agaaattggg gggcaccaag 1200
 gtgttaattg caagcgtgca aggttcaaag agaaggaagc ttcgagtata ccttcattgc 1260
 acaaacactg acaatccaag gtataaagaa ggagatttaa ctctgtatgc cataaacctc 1320
 cataatgtca ccaagtactt gcggttacc ctaacttttt ctaacaagca agtggataaa 1380
 taccttctaa gacctttggg acctcatgga ttactttcca aatctgtcca actcaatggt 1440
 ctaactctaa agatgggtgga tgatcaaacc ttgccacctt taatggaaaa acctctccgg 1500
 ccaggaagtt cactgggctt gccagctttc tcatatagtt tttttgtgat aagaaatgcc 1560
 aaagttgctg cttgcatctg a 1581

<210> 29
 <211> 570
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> hep TEV110-158

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 35 40 45
 Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn
 50 55 60
 Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu
 65 70 75 80
 Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly
 85 90 95
 Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Gly Ser Gly
 100 105 110
 Ser Glu Asn Leu Tyr Phe Gln Gly Ser Gly Ser Thr Phe Glu Glu Arg
 115 120 125

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Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys Lys Tyr Gly Ser
130 135 140
Ile Pro Pro Asp Val Glu Lys Leu Arg Leu Glu Trp Pro Tyr Gln
145 150 155 160
Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Ser Gly Ser Gly Glu Asn
165 170 175
Leu Tyr Phe Gln Gly Ser Gly Ser Lys Lys Phe Lys Asn Ser Thr Tyr
180 185 190
Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe Ala Asn Cys Ser Gly
195 200 205
Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Ala Asp Leu
210 215 220
Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser
225 230 235 240
Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe
245 250 255
Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser Gln Leu Gly Glu Asp
260 265 270
Phe Ile Gln Leu His Lys Leu Leu Arg Lys Ser Thr Phe Lys Asn Ala
275 280 285
Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg Arg Lys Thr Ala Lys
290 295 300
Met Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Val
305 310 315 320
Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr Ala Thr Arg Glu Asp
325 330 335
Phe Leu Asn Pro Asp Val Leu Asp Ile Phe Ile Ser Ser Val Gln Lys
340 345 350
Val Phe Gln Val Val Glu Ser Thr Arg Pro Gly Lys Lys Val Trp Leu
355 360 365
Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asp
370 375 380
Thr Phe Ala Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala
385 390 395 400
Arg Met Gly Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly
405 410 415
Asn Tyr His Leu Val Asp Glu Asn Phe Asp Pro Leu Pro Asp Tyr Trp
420 425 430
Leu Ser Leu Leu Phe Lys Lys Leu Val Gly Thr Lys Val Leu Met Ala
435 440 445
Ser Val Gln Gly Ser Lys Arg Arg Lys Leu Arg Val Tyr Leu His Cys
450 455 460
Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly Asp Leu Thr Leu Tyr
465 470 475 480
Ala Ile Asn Leu His Asn Val Thr Lys Tyr Leu Arg Leu Pro Tyr Pro
485 490 495
Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu Leu Arg Pro Leu Gly Pro
500 505 510
His Gly Leu Leu Ser Lys Ser Val Gln Leu Asn Gly Leu Thr Leu Lys
515 520 525
Met Val Asp Asp Gln Thr Leu Pro Pro Leu Met Glu Lys Pro Leu Arg
530 535 540
Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe Ser Tyr Ser Phe Phe Val
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Ile Arg Asn Ala Lys Val Ala Ala Cys Ile
565 570

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<210> 30

<211> 1668

<212> DNA

<213> Artificial Sequence

<220>

<223> hep TEV110

<400> 30

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<210> 31

<211> 556

<212> PRT

<213> Artificial Sequence

<220>

<223> hep TEV110

<400> 31

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Leu Leu Gly Pro Leu Gly Pro Leu Ser Pro Gly Ala Leu Pro Arg Pro
20      25      30
Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro
35      40      45
Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn
50      55      60
Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu
65      70      75      80
Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly
85      90      95
Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Gly Ser Gly
100     105     110
Ser Glu Asn Leu Tyr Phe Gln Gly Ser Gly Ser Thr Phe Glu Glu Arg
115     120     125
Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys Lys Tyr Gly Ser
130     135     140
Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu Trp Pro Tyr Gln
145     150     155     160
Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys Phe Lys Asn Ser
165     170     175
Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe Ala Asn Cys

```

Ser	Gly	Leu	Asp	Leu	Ile	Phe	Gly	Leu	Asn	Ala	Leu	Leu	Arg	Thr	Ala
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Asp	Leu	Gln	Trp	Asn	Ser	Ser	Asn	Ala	Gln	Leu	Leu	Asp	Tyr	Cys	
185	200	215	230	245	260	275	290	305	320	335	350	365	380	395	410
Ser	Ser	Lys	Gly	Tyr	Asn	Ile	Ser	Trp	Glu	Leu	Gly	Asn	Glu	Pro	Asn
190	205	220	235	250	265	280	295	310	325	340	355	370	385	400	415
Ser	Phe	Leu	Lys	Lys	Ala	Asp	Ile	Phe	Ile	Asn	Gly	Ser	Gln	Leu	Gly
195	210	225	240	255	270	285	300	315	330	345	360	375	390	405	420
Glu	Asp	Phe	Ile	Gln	Leu	His	Lys	Leu	Leu	Arg	Lys	Ser	Thr	Phe	Lys
200	215	230	245	260	275	290	305	320	335	350	365	380	395	410	425
Asn	Ala	Lys	Leu	Tyr	Gly	Pro	Asp	Val	Gly	Gln	Pro	Arg	Arg	Lys	Thr
205	220	235	250	265	280	295	310	325	340	355	370	385	400	415	430
Ala	Lys	Met	Leu	Lys	Ser	Phe	Leu	Lys	Ala	Gly	Gly	Glu	Val	Ile	Asp
210	225	240	255	270	285	300	315	330	345	360	375	390	405	420	435
Ser	Val	Thr	Trp	His	His	Tyr	Tyr	Leu	Asn	Gly	Arg	Thr	Ala	Thr	Arg
215	230	245	260	275	290	305	320	335	350	365	380	395	410	425	440
Glu	Asp	Phe	Leu	Asn	Pro	Asp	Val	Leu	Asp	Ile	Phe	Ile	Ser	Ser	Val
220	235	250	265	280	295	310	325	340	355	370	385	400	415	430	445
Gln	Lys	Val	Phe	Gln	Val	Val	Glu	Ser	Thr	Arg	Pro	Gly	Lys	Lys	Val
225	240	255	270	285	300	315	330	345	360	375	390	405	420	435	450
Trp	Leu	Gly	Glu	Thr	Ser	Ser	Ala	Tyr	Gly	Gly	Gly	Ala	Pro	Leu	Leu
230	245	260	275	290	305	320	335	350	365	380	395	410	425	440	455
Ser	Asp	Thr	Phe	Ala	Ala	Gly	Phe	Met	Trp	Leu	Asp	Lys	Leu	Gly	Leu
235	250	265	280	295	310	325	340	355	370	385	400	415	430	445	460
Ser	Ala	Arg	Met	Gly	Ile	Glu	Val	Val	Met	Arg	Gln	Val	Phe	Phe	Gly
240	255	270	285	300	315	330	345	360	375	390	405	420	435	450	465
Ala	Gly	Asn	Tyr	His	Leu	Val	Asp	Glu	Asn	Phe	Asp	Pro	Leu	Pro	Asp
245	260	275	290	305	320	335	350	365	380	395	410	425	440	455	470
Tyr	Trp	Leu	Ser	Leu	Leu	Phe	Lys	Lys	Leu	Val	Gly	Thr	Lys	Val	Leu
250	265	280	295	310	325	340	355	370	385	400	415	430	445	460	475
Met	Ala	Ser	Val	Gln	Gly	Ser	Lys	Arg	Arg	Lys	Leu	Arg	Val	Tyr	Leu
255	270	285	300	315	330	345	360	375	390	405	420	435	450	465	480
His	Cys	Thr	Asn	Thr	Asp	Asn	Pro	Arg	Tyr	Lys	Glu	Gly	Asp	Leu	Thr
260	275	290	305	320	335	350	365	380	395	410	425	440	455	470	485
Leu	Tyr	Ala	Ile	Asn	Leu	His	Asn	Val	Thr	Lys	Tyr	Leu	Arg	Leu	Pro
265	280	295	310	325	340	355	370	385	400	415	430	445	460	475	490
Tyr	Pro	Phe	Ser	Asn	Lys	Gln	Val	Asp	Lys	Tyr	Leu	Leu	Arg	Pro	Leu
270	285	300	315	330	345	360	375	390	405	420	435	450	465	480	495
Gly	Pro	His	Gly	Leu	Leu	Ser	Lys	Ser	Val	Gln	Leu	Asn	Gly	Leu	Thr
275	290	305	320	335	350	365	380	395	410	425	440	455	470	485	500
Leu	Lys	Met	Val	Asp	Asp	Gln	Thr	Leu	Pro	Pro	Leu	Met	Glu	Lys	Pro
280	295	310	325	340	355	370	385	400	415	430	445	460	475	490	505
Leu	Arg	Pro	Gly	Ser	Ser	Leu	Gly	Leu	Pro	Ala	Phe	Ser	Tyr	Ser	Phe
285	300	315	330	345	360	375	390	405	420	435	450	465	480	495	510
Phe	Val	Ile	Arg	Asn	Ala	Lys	Val	Ala	Ala	Cys	Ile				
290	305	320	335	350	365	380	395	410	425	440	455	470	485	500	515

<210> 32

<211> 1710

<212> DNA

<213> Artificial Sequence

<220>

<223> hep TEV110/158

<400> 32

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ctggacttct	tcaccagga	gccgctgcac	ctgggtgagcc	cctcgttcct	gtccgtcacc	180
attgacgcca	acctggccac	ggaccgcg	ttcctcatcc	tcctgggttc	tcctgggttc	240
cgtacattgg	ccagaggctt	gtctcctgcg	tacctgaggt	ttggtggcac	caagacagac	300
ttcctaattt	tcgatcccaa	gaaggaaggc	agcggatctg	agaacctgta	cttccagggt	360

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gagcaattgc tactccgaga acactaccag tctggatccg gtgaaaatct ctattttcag 540
ggctcaggaa gtaaaaagtt caagaacagc acctactcaa gaagctctgt agatgtgcta 600
tacacttttg caaactgctc aggactggac ttgatctttg gcctaaatgc gttattaaga 660
acagcagatt tgcagtggaa cagttctaata gctcagttgc tcctggacta ctgctcttcc 720
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caactcaatg gtctaactct aaagatgggt gatgatcaaa ccttgccacc tttaattggaa 1620
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ataagaaatg ccaaagttgc tgcttgcac 1710

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<210> 33
 <211> 174
 <212> PRT
 <213> Homo Sapiens

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<400> 33
Gln Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro Leu His
1 5 10 15
Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn Leu Ala
20 25 30
Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu Arg Thr
35 40 45
Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys
50 55 60
Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr Phe Glu Glu
65 70 75 80
Arg Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys Lys Tyr Gly
85 90 95
Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu Trp Pro Tyr
100 105 110
Gln Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys Phe Lys Asn
115 120 125
Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe Ala Asn
130 135 140
Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr
145 150 155 160
Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu
165 170

```

<210> 34
 <211> 174
 <212> PRT
 <213> Mus Musculus

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<400> 34
Thr Asp Asp Val Val Asp Leu Glu Phe Tyr Thr Lys Arg Pro Leu Arg
1 5 10 15
Ser Val Ser Pro Ser Phe Leu Ser Ile Thr Ile Asp Ala Ser Leu Ala
20 25 30

```

```

Thr Asp Pro Arg Phe Leu Thr Phe Leu Gly Ser Pro Arg Leu Arg Ala
      35      40      45
Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys
      50      55      60
Thr Asp Phe Leu Ile Phe Asp Pro Asp Lys Glu Pro Thr Ser Glu Glu
      65      70      75      80
Arg Ser Tyr Trp Lys Ser Gln Val Asn His Asp Ile Cys Arg Ser Glu
      85      90      95
Pro Val Ser Ala Ala Val Leu Arg Lys Leu Gln Val Glu Trp Pro Phe
      100      105      110
Gln Glu Leu Leu Leu Arg Glu Gln Tyr Gln Lys Glu Phe Lys Asn
      115      120      125
Ser Thr Tyr Ser Arg Ser Ser Val Asp Met Leu Tyr Ser Phe Ala Lys
      130      135      140
Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr
      145      150      155      160
Pro Asp Leu Arg Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu
      165      170

```

<210> 35
 <211> 174
 <212> PRT
 <213> Bos taurus

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<400> 35
Ala Asp Asp Ala Ala Glu Leu Glu Phe Phe Thr Glu Arg Pro Leu His
1      5      10      15
Leu Val Ser Pro Ala Phe Leu Ser Phe Thr Ile Asp Ala Asn Leu Ala
      20      25      30
Thr Asp Pro Arg Phe Phe Thr Phe Leu Gly Ser Ser Lys Leu Arg Thr
      35      40      45
Leu Ala Arg Gly Leu Ala Pro Ala Tyr Leu Arg Phe Gly Gly Asn Lys
      50      55      60
Gly Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Pro Ala Phe Glu Glu
      65      70      75      80
Arg Ser Tyr Trp Leu Ser Gln Ser Asn Gln Asp Ile Cys Lys Ser Gly
      85      90      95
Ser Ile Pro Ser Asp Val Glu Glu Lys Leu Arg Leu Glu Trp Pro Phe
      100      105      110
Gln Glu Gln Val Leu Leu Arg Glu Gln Tyr Gln Lys Lys Phe Thr Asn
      115      120      125
Ser Thr Tyr Ser Arg Ser Ser Val Asp Met Leu Tyr Thr Phe Ala Ser
      130      135      140
Cys Ser Gly Leu Asn Leu Ile Phe Gly Val Asn Ala Leu Leu Arg Thr
      145      150      155      160
Thr Asp Met His Trp Asp Ser Ser Asn Ala Gln Leu Leu Leu
      165      170

```

<210> 36
 <211> 173
 <212> PRT
 <213> Gallus Gallus

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<400> 36
Pro Arg Arg Thr Ala Glu Leu Gln Leu Gly Leu Arg Glu Pro Ile Gly
1      5      10      15
Ala Val Ser Pro Ala Phe Leu Ser Leu Thr Leu Asp Ala Ser Leu Ala
      20      25      30
Arg Asp Pro Arg Phe Val Ala Leu Arg His Pro Lys Leu His Thr
      35      40      45
Leu Ala Ser Gly Leu Ser Pro Gly Phe Leu Arg Phe Gly Gly Thr Ser
      50      55      60

```

```

Thr Asp Phe Leu Ile Phe Asn Pro Asn Lys Asp Ser Thr Trp Glu Glu
65      70      75      80
Lys Val Leu Ser Glu Phe Gln Ala Lys Asp Val Cys Glu Ala Trp Pro
85      90      95
Ser Phe Ala Val Val Pro Lys Leu Leu Leu Thr Gln Trp Pro Leu Gln
100      105      110
Glu Lys Leu Leu Ala Glu His Ser Trp Lys Lys His Lys Asn Thr
115      120      125
Thr Ile Thr Arg Ser Thr Leu Asp Ile Leu His Thr Phe Ala Ser Ser
130      135      140
Ser Gly Phe Arg Leu Val Phe Gly Leu Asn Ala Leu Leu Arg Arg Ala
145      150      155      160
Gly Leu Gln Trp Asp Ser Ser Asn Ala Lys Gln Leu Leu
165      170

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<210> 37
 <211> 189
 <212> PRT
 <213> Homo Sapiens

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<400> 37
Glu Lys Thr Leu Ile Leu Leu Asp Val Ser Thr Lys Asn Pro Val Arg
1      5      10      15
Thr Val Asn Glu Asn Phe Leu Ser Leu Gln Leu Asp Pro Ser Ile Ile
20      25      30
His Asp Gly Trp Leu Asp Phe Leu Ser Ser Lys Arg Leu Val Thr Leu
35      40      45
Ala Arg Gly Leu Ser Pro Ala Phe Leu Arg Phe Gly Gly Lys Arg Thr
50      55      60
Asp Phe Leu Gln Phe Gln Asn Leu Arg Asn Pro Ala Lys Ser Arg Gly
65      70      75      80
Gly Pro Gly Pro Asp Tyr Tyr Leu Lys Asn Tyr Glu Asp Asp Ile Val
85      90      95
Arg Ser Asp Val Ala Leu Asp Lys Gln Lys Gly Cys Lys Ile Ala Gln
100      105      110
His Pro Asp Val Met Leu Glu Leu Gln Arg Glu Lys Ala Ala Gln Met
115      120      125
His Leu Val Leu Leu Lys Glu Gln Phe Ser Asn Thr Tyr Ser Asn Leu
130      135      140
Ile Leu Thr Ala Arg Ser Leu Asp Lys Leu Tyr Asn Ser Ala Asp Cys
145      150      155      160
Ser Gly Leu His Leu Ile Phe Ala Leu Asn Ala Leu Arg Arg Asn Pro
165      170      175
Asn Asn Ser Trp Asn Ser Ser Ser Ala Leu Ser Leu Leu
180      185

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<210> 38
 <211> 151
 <212> PRT
 <213> Bombyx Mori

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<400> 38
Val Arg Tyr Phe Val Thr Ile Asn Glu Asn Gln Glu Asp Ile Lys Leu
1      5      10      15
Ile Ser Glu Asp Phe Leu Ser Phe Gly Ile Asp Thr Ile Glu Ile Glu
20      25      30
Asn Tyr Asn Arg Ile Asn Tyr Ser Asp Thr Arg Leu Arg Glu Leu Ala
35      40      45
Ala Ala Leu Ser Pro Ala Arg Leu Arg Leu Gly Gly Thr Met Ser Glu
50      55      60
Arg Leu Ile Phe Ser Lys Glu Asn Ile Pro Ile Ser Cys His Asn Cys
65      70      75      80

```

Ser	Tyr	Lys	Ser	Tyr 85	Pro	Lys	Ser	Leu	Cys 90	Gln	Leu	Ile	Glu	Lys 95	Pro
Cys	Lys	His	Lys 100	His	Lys	Phe	Leu	Pro 105	Phe	Phe	Ile	Met	Thr 110	Gly	Asn
Glu	Trp	Asn 115	Gln	Ile	Asn	Asp	Phe 120	Cys	Arg	Lys	Thr	Asn 125	Leu	Lys	Leu
Leu	Phe 130	Ser	Leu	Asn	Ala	Met 135	Leu	Arg	Asp	Asn	His 140	Gly	Trp	Asn	Glu
Lys 145	Asn	Ala	Arg	Glu	Leu	Ile 150									

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<210> 39
<211> 147
<212> PRT
<213> Hirudinaria manillensis
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```
<400> 39  
Lys Asn Val Ile Ala Ser Val Ser Glu Ser Phe His Gly Val Ala Phe  
1      5      10     15  
Asp Ala Ser Leu Phe Ser Pro Lys Gly Pro Trp Ser Phe Val Asn Ile  
    20     25     30  
Thr Ser Pro Lys Leu Phe Lys Leu Leu Glu Gly Leu Ser Pro Gly Tyr  
    35     40     45  
Phe Arg Val Gly Gly Thr Phe Ala Asn Trp Leu Phe Asp Leu Asp  
    50     55     60  
Glu Asn Asn Lys Trp Lys Asp Tyr Trp Ala Phe Lys Asp Lys Thr Pro  
65     70     75     80  
Glu Thr Ala Thr Ile Thr Arg Arg Trp Leu Phe Arg Lys Gln Asn Asn  
    85     90     95  
Leu Lys Lys Glu Thr Phe Asp Asp Leu Val Lys Leu Thr Lys Gly Ser  
    100   105   110  
Lys Met Arg Leu Leu Phe Asp Leu Asn Ala Glu Val Arg Thr Gly Tyr  
    115   120   125  
Glu Ile Gly Lys Lys Thr Thr Ser Thr Trp Asp Ser Ser Glu Ala Glu  
    130   135   140  
Lys Leu Phe  
145
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<210> 40
<211> 150
<212> PRT
<213> Scutellaria baicallensis
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<400>	40															
Asn	Tyr	Val	Cys	Ala	Thr	Leu	Asp	Leu	Trp	Pro	Pro	Thr	Lys	Cys	Asn	
1				5					10					15		
Tyr	Gly	Asn	Cys	Pro	Trp	Gly	Lys	Ser	Ser	Phe	Leu	Asn	Leu	Asp	Leu	
			20					25					30			
Asn	Asn	Asn	Ile	Ile	Arg	Asn	Ala	Val	Lys	Glu	Phe	Ala	Pro	Leu	Lys	
		35					40					45				
Leu	Arg	Phe	Gly	Gly	Thr	Leu	Gln	Asp	Arg	Leu	Val	Tyr	Gln	Thr	Ser	
	50					55					60					
Arg	Asp	Glu	Pro	Cys	Asp	Ser	Thr	Phe	Tyr	Asn	Asn	Thr	Asn	Leu	Ile	
65					70					75					80	
Leu	Asp	Phe	Ser	His	Ala	Cys	Leu	Ser	Leu	Asp	Arg	Trp	Asp	Glu	Ile	
			85						90					95		
Asn	Gln	Phe	Ile	Leu	Glu	Thr	Gly	Ser	Glu	Ala	Val	Phe	Gly	Leu	Asn	
			100					105					110			
Ala	Leu	Arg	Gly	Lys	Thr	Val	Glu	Ile	Lys	Gly	Ile	Ile	Lys	Asp	Gly	
		115					120					125				
Gln	Tyr	Leu	Gly	Glu	Thr	Thr	Thr	Ala	Val	Gly	Glu	Trp	Asp	Tyr	Ser	
	130					135					140					

Asn Ser Lys Phe Leu Ile
145 150

<210> 41
<211> 138
<212> PRT
<213> Arabidopsis thaliana

<400> 41
Asn Phe Val Cys Ala Thr Leu Asp Trp Trp Pro His Asp Lys Cys Asn
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Tyr Asp Gln Cys Pro Trp Gly Tyr Ser Ser Val Ile Asn Met Asp Leu
20 25 30
Thr Arg Pro Leu Leu Thr Lys Ala Ile Lys Ala Phe Lys Pro Leu Arg
35 40 45
Ile Arg Ile Gly Gly Ser Leu Gln Asp Gln Val Ile Tyr Asp Val Gly
50 55 60
Asn Leu Lys Thr Pro Cys Arg Pro Phe Gln Lys Met Asn Ser Gly Leu
65 70 75 80
Phe Gly Phe Ser Lys Gly Cys Leu His Met Lys Arg Trp Asp Glu Leu
85 90 95
Asn Ser Phe Leu Thr Ala Thr Gly Ala Val Val Thr Phe Gly Leu Asn
100 105 110
Ala Leu Arg Gly Arg His Lys Leu Arg Gly Lys Ala Trp Gly Gly Ala
115 120 125
Trp Asp His Ile Asn Thr Gln Asp Phe Leu
130 135

<210> 42
<211> 138
<212> PRT
<213> Arabidopsis thaliana

<400> 42
Asp Phe Ile Cys Ala Thr Leu Asp Trp Trp Pro Pro Glu Lys Cys Asp
1 5 10 15
Tyr Gly Ser Cys Ser Trp Asp His Ala Ser Ile Leu Asn Leu Asp Leu
20 25 30
Asn Asn Val Ile Leu Gln Asn Ala Ile Lys Ala Phe Ala Pro Leu Lys
35 40 45
Ile Arg Ile Gly Gly Thr Leu Gln Asp Ile Val Ile Tyr Glu Thr Pro
50 55 60
Asp Ser Lys Gln Pro Cys Leu Pro Phe Thr Lys Asn Ser Ser Ile Leu
65 70 75 80
Phe Gly Tyr Thr Gln Gly Cys Leu Pro Met Arg Arg Trp Asp Glu Leu
85 90 95
Asn Ala Phe Phe Arg Lys Thr Gly Thr Lys Val Ile Phe Gly Leu Asn
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Ala Leu Ser Gly Arg Ser Ile Lys Ser Asn Gly Glu Ala Ile Gly Ala
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Trp Asn Tyr Thr Asn Ala Glu Ser Phe Ile
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<212> PRT
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Tyr Asp Gln Cys Pro Trp Gly Tyr Ala Ser Leu Ile Asn Leu Asn Leu
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Ala Ser Pro Leu Leu Ala Lys Ala Ile Gln Ala Phe Arg Thr Leu Arg
      35      40      45
Ile Arg Ile Gly Gly Ser Leu Gln Asp Gln Val Ile Tyr Asp Val Gly
      50      55      60
Asp Leu Lys Thr Pro Cys Thr Gln Phe Lys Lys Thr Asp Asp Gly Leu
      65      70      75      80
Phe Gly Phe Ser Glu Gly Cys Leu Tyr Met Lys Arg Trp Asp Glu Val
      85      90      95
Asn His Phe Phe Asn Ala Thr Gly Ala Ile Val Thr Phe Gly Leu Asn
      100      105      110
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Trp Asp His Thr Asn Thr Gln Asp Phe Met
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Ala Phe Lys Asp Lys Thr Pro
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